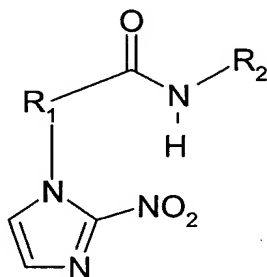


This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims**

**Claim 1 - 5 (canceled)**

**Claim 6 (previously presented)** A method for the synthesis of a [ $^{18}\text{F}$ ]-labeled perfluorinated-nitroaromatic compound having the formula:



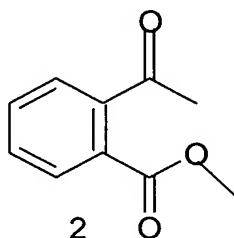
wherein R<sub>1</sub> is CH<sub>2</sub> and R<sub>2</sub> is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula CHXCX<sub>2</sub>CY<sub>3</sub> where X is halogen or hydrogen and Y is fluorine, comprising

(1) perfluorinating a first intermediate which is an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group having a carboxyl function transformed into a dithioester function or a synthetically equivalent persulphurated moiety thereby obtaining a [ $^{18}\text{F}$ ]-labeled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group as a second intermediate and

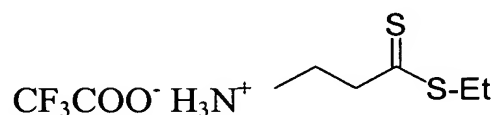
(2) deprotecting the nitrogen function of said second intermediate, resulting in a [ $^{18}\text{F}$ ] labeled perfluoroalkyl amine derivative, and coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [ $^{18}\text{F}$ ] labeled perfluoroalkyl amine derivative.

**Claim 7 (currently amended)** A method for the synthesis of a compound according to claim 6, wherein step (1) comprises ~~comprising~~:

- a) adding a THF solution of a compound of formula 2 to a suspension of PYBOP in THF followed by Et<sub>3</sub>N,



- b) adding an amine of formula 1 and Et<sub>3</sub>N to the solution obtained in step (a),



- c) adding a catalytic amount to the solution obtained in step (b) of pTsOH and refluxing the solution,
- d) cooling the solution obtained after step (c) at ambient temperature and adding a sodium bicarbonate solution,
- e) extracting the product obtained after step (d) with ethyl acetate and drying and concentrating the product with ethyl acetate,
- f) purifying the residue obtained after step (e) by column chromatography on silica gel,
- g) removing traces of water by washing the product of step (f) with trifluoroacetic anhydride,
- h) reacting a persulphurated derivative obtained from step (g) with a suitable labeled perfluorinating agent and a suitable oxidant resulting in a compound having a high yield of fluorine ~~fluor~~ atom incorporation,

and wherein step (2) comprises:

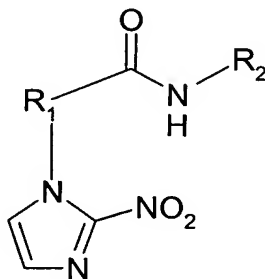
- i) deprotecting the nitrogen function, resulting in a perfluoroalkyl amine derivative, and
- j) coupling the perfluoroalkyl amine derivative obtained in step (i) with an activated form of 2-(2-nitro-imidazol-1-yl) acetic acid, resulting in the [ $^{18}\text{F}$ ]-labeled ~~or~~ perfluorinated-nitroaromatic compound.

**Claim 8 (currently amended)** A method according to claim 7 wherein hydrogen fluoride/pyridine complex (HF-Pyridine) is used as a perfluorinating agent and 1,3-dibromo-5,5-dimethylhydantoin (DBH) is used as an oxidant resulting in a compound having a high yield of fluorine ~~fluor~~ atom incorporation.

**Claims 9 - 25 (canceled)**

**Claim 26 (currently amended)** A method for the detection of tissue hypoxia in a patient comprising:

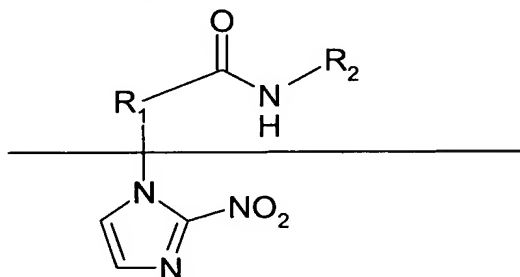
- producing ~~according to the method of claim 6~~ a [ $^{18}\text{F}$ ]-labeled perfluorinated-nitroaromatic compound having the formula:



wherein  $\text{R}_1$  is  $\text{CH}_2$  and  $\text{R}_2$  is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula  $\text{CHXCX}_2\text{CY}_3$  where X is halogen or hydrogen and Y is fluorine by (1) perfluorinating a first intermediate which is an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group having a carboxyl function

transformed into a dithioester function or a synthetically equivalent persulphurated moiety thereby obtaining a [ $^{18}\text{F}$ ]-labeled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group as a second intermediate and

(2) deprotecting the nitrogen function of said second intermediate, resulting in a [ $^{18}\text{F}$ ] labeled perfluoroalkyl amine derivative, and coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [ $^{18}\text{F}$ ] labeled perfluoroalkyl amine derivative ~~coupling 2-(2-nitro-imidazol-1-yl)acetic acid with a [ $^{18}\text{F}$ ]-labeled perfluoroalkyl amine derivative according to the method of claim 6;~~

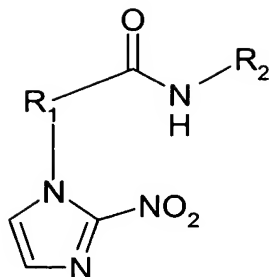


and - quantifying tissue hypoxia in said patient by imaging ~~imagining~~ said patient ~~patent~~ after having introduced said [ $^{18}\text{F}$ ] labeled nitromidazole compound into said patient.

**Claim 27 (original)** A method according to claim 26 wherein the detection technique used in said method is positron emission tomography.

**Claim 28 (currently amended)** A method for the detection of tissue hypoxia in a tissue comprising:

- producing ~~according to the method of claim 6~~ a [ $^{18}\text{F}$ ]-labeled perfluorinated-nitroaromatic compound having the formula:

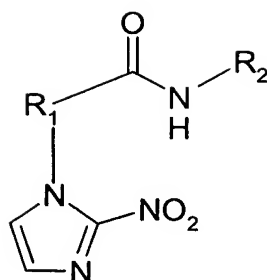


wherein  $R_1$  is  $CH_2$  and  $R_2$  is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula  $CHXCX_2CY_3$  where X is halogen or hydrogen and Y is fluorine by (1) perfluorinating a first intermediate which is an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group having a carboxyl function transformed into a dithioester function or a synthetically equivalent persulphurated moiety thereby obtaining a [ $^{18}F$ ]-labeled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group as a second intermediate and  
(2) deprotecting the nitrogen function of said second intermediate, resulting in a [ $^{18}F$ ] labeled perfluoroalkyl amine derivative, and coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [ $^{18}F$ ] labeled perfluoroalkyl amine derivative coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [ $^{18}F$ ]-labeled perfluoroalkyl amine derivative;

- introducing said [ $^{18}F$ ] labeled nitroimidazole compound of claim 6 into a patient,
- removing a tissue sample from said patient, and
- analysing the emission in said tissue sample by autoradiography.

**Claim 29 (currently amended)** A method for the detection of an [ $^{18}F$ ] labeled bioactive compound in a patient comprising:

- producing ~~according to the method of claim 6~~ a [ $^{18}F$ ]-labeled perfluorinated-nitroaromatic compound having the formula:



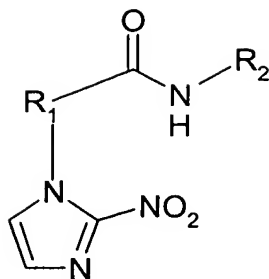
wherein  $R_1$  is  $CH_2$  and  $R_2$  is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula  $CHXCX_2CY_3$  where X is halogen or hydrogen and Y is fluorine by (1) perfluorinating a first intermediate which is an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group having a carboxyl function transformed into a dithioester function or a synthetically equivalent persulphurated moiety thereby obtaining a [ $^{18}F$ ]-labeled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group as a second intermediate and

(2) deprotecting the nitrogen function of said second intermediate, resulting in a [ $^{18}F$ ] labeled perfluoroalkyl amine derivative, and coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [ $^{18}F$ ] labeled perfluoroalkyl amine derivative coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [ $^{18}F$ ]-labeled perfluoroalkyl amine derivative;

- introducing said [ $^{18}F$ ] labeled bioactive compound ~~according to claim 6~~ into said patient,
- imaging the presence of said [ $^{18}F$ ] labeled bioactive compound in said patient, and
- optionally, quantifying the presence of said [ $^{18}F$ ] labeled bioactive compound in said patient.

**Claim 30 (currently amended)** A method for the detection of [ $^{18}F$ ] labeled bioactive compound in a tissue comprising:

- producing ~~according to the method of claim 6~~ a [ $^{18}F$ ]-labeled perfluorinated-nitroaromatic compound having the formula:



wherein  $R_1$  is  $CH_2$  and  $R_2$  is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula  $CHXCX_2CY_3$  where X is halogen or hydrogen and Y is fluorine by (1) perfluorinating a first intermediate which is an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group having a carboxyl function transformed into a dithioester function or a synthetically equivalent persulphurated moiety thereby obtaining a [ $^{18}F$ ]-labeled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group as a second intermediate and

(2) deprotecting the nitrogen function of said second intermediate, resulting in a [ $^{18}F$ ] labeled perfluoroalkyl amine derivative, and coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [ $^{18}F$ ] labeled perfluoroalkyl amine derivative coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [ $^{18}F$ ] labeled perfluoroalkyl amine derivative;

- introducing an [ $^{18}F$ ] labeled bioactive compound of claim 6 into a patient,
- taking a tissue sample from said patient, and
- analysing the emission in said tissue sample by autoradiography.

Claim 31 (canceled)

Claim 32 (currently amended) A method according to claim 6, wherein the compound has a specific radioactivity of 1 to 30 Ci/mmol.

Claim 33 (currently amended) A method according to claim 6, wherein the compound is has the formula 2-(2-nitro-1H-imidazol-1-yl)-N-(3,3,3-trifluoropropyl) acetamide ([ $^{18}F$ ]-EF3).

Claim 34 (**currently amended**)      A method according to claim 6, wherein the compound ~~is has the formula~~ 2(2-nitro-1H-imidazol-1-yl)-N-2,2,3,3,3-pentafluoropropyl acetamide ([<sup>18</sup>F]-EF5).

Claim 35 (**canceled**)